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## Mammalian artificial chromosomes as tools for gene therapy.

**Vos JM.**

Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill 27599-7295, USA. [vos@med.unc.edu](mailto:vos@med.unc.edu)

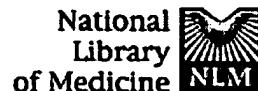
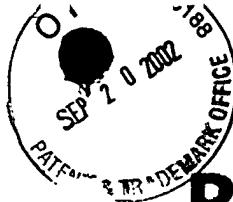
Mammalian artificial chromosomes (MACs) represent powerful tools for human gene therapy and animal transgenesis. First-generation linear genomic human artificial chromosomes (HACs) and circular chimeric genomic/viral mouse artificial episomal chromosomes (MAECs) have been developed. HACs have been shuttled from human into mouse embryonal stem cells and human trans-chromosomal mice have been generated. The potential of new genetic cis-elements and epigenetic phenomena for de novo segregation and replication activities on MACs are points for discussion. Once the size and delivery constraints of HACs are circumvented, therapeutic applications will be numerous, particularly for recessive syndromes involving large genes and multigenic diseases.

### Publication Types:

- Review
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## Mammalian artificial chromosomes: a new tool for gene therapy.

Huxley C.

Department of Biochemistry and Molecular Genetics, St Mary's Hospital Medical School, London, UK.

Effective therapy by *in vivo* delivery of DNA requires efficient delivery, long-term maintenance of the DNA that is delivered and physiological levels of expression of the therapeutic gene. Full levels of physiologically controlled expression can be obtained after transfer of intact genes on fragments of DNA hundreds of kilobases in size, as has been demonstrated by the transfer of yeast artificial chromosomes into transgenic mice. Long-term maintenance of input DNA could be achieved if the DNA carried replication origins, a centromere and telomeres to allow maintenance and segregation in mammalian cells, and there has been recent progress towards cloning these elements. These features could be combined as a mammalian artificial chromosome which would confer full levels of controlled expression as well as being maintained in any cell into which it was introduced. Methods which would allow delivery of such large fragments of DNA include liposomes and receptor-mediated uptake, both of which have been shown to work *in vivo*, making such large constructs potentially applicable for use in gene therapy.

### Publication Types:

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